Journal of Forensic and Legal Medicine 16 (2009) 499–500

Contents lists available at ScienceDirect

Journal of Forensic and Legal Medicine

journal homepage: www.elsevier.com/jflm

Postcard from Sweden

Post-mortem toxicology is not quackery when done by qualified practitioners

To the editor,

The rather provocative title of Steven B. Karch's postcard from America (*Is postmortem toxicology quackery?*) should have raised a few eyebrows among practicing forensic toxicologists.[1] Surprisingly, his postcard and opinions have, to my knowledge, not been answered. This prompted a postcard from Sweden to highlight some errors and omissions in the material submitted by Dr. Karch.

As a matter of interest, the word quack comes from the Dutch *kwakken*, which means to prattle, chatter or sound like a duck, a phrase commonly associated with quack-salving physicians.[2] In today's parlance a quack is synonymous with a mountebank or charlatan.

What exactly motivated Dr. Karch's attack on the discipline of forensic toxicology and by implication forensic toxicologists is hard to comprehend. However, one gets the impression that it had to do with testimony proffered by defence and prosecution experts in a murder trial in the UK. The expert witnesses in the case seemingly had differences of opinion about the concentrations of morphine and its metabolites in blood from a heroin-overdose death and how these should be interpreted. This situation is by no means unusual in the adversarial system of justice and calls for a re-think about the way that expert medical and forensic evidence is presented to the jury.

A physician, Dr. David Moor, was charged with murdering a terminally ill cancer patient (85 y old) by giving him a massive dose of heroin (diamorphine). Exact details of the toxicological results were unfortunately not reported in Dr. Karch's letter. Nevertheless, it appears that the concentration of free morphine to metabolites in post-mortem blood (sampling site not mentioned) was unusually high. This was interpreted by the prosecution as compelling evidence that a massive overdose of heroin had been given and that death occurred before much of the morphine (major metabolite of heroin) had been transformed into its glucuronide conjugates.

Whether the heroin metabolite 6-acetyl morphine was analyzed or detected in blood was not mentioned in Karch's letter. Neither did he provide information about the analytical methods used, the site of sampling blood nor whether morphine-3-glucuronide and morphine-6-glucuronide were determined separately. I am uncertain what prompted Dr. Karch to write about this case without at the same time providing all relevant toxicological information to allow an independent assessment.

It is widely known that the concentrations of morphine determined in blood from heroin-related deaths and heroin-related *overdose* deaths are hard to interpret.[3] There is a lack of association between the concentrations of free morphine in blood and the mode of death in heroin users.[4] This might be interpreted to mean a loss of tolerance to opiates or perhaps, more importantly, concomitant use of other psychoactive substances, such as benzodiazepines or ethanol, factors known to exaggerate the toxicity of opiates.[5]

The defence expert in the Dr. Moor trial raised the notion that micro-organisms (*Escherichia coli*) in the bowel might have split the conjugates of morphine (morphine-3-glucuronide and morphine-6-glucuronde) converting them back to free morphine after death before an autopsy was performed. This was offered as a possible explanation for the high concentration ratio of free-morphine to metabolites in the autopsy blood samples. Although some published studies are available about the stability of morphine glucuronides in post-mortem blood, none of this work was done by Dr. Karch.[6,7]

Skopp et al.[6] reported an in-vitro study with post-mortem blood spiked with morphine and its glucuronide metabolites. They found a ~30% increase in free-morphine concentration after storage of blood samples at room temperature exposed to light for 20 days. The likelihood that the conjugates of morphine undergo hydrolysis to free-morphine in cadavers stored for various periods of time at room temperature has never been investigated. The propensity for morphine, morphine-3-glucurnide and morphine-6-glucurnide to re-distribute in body fluids after death was, however, investigated in 40 heroin-related deaths.[7] The authors concluded that significant postmortem redistribution of morphine and its conjugates was unlikely when the post-mortem interval was up to 59 h.[7] Karch's theory that the concentrations of free-morphine in autopsy blood from Mr. Liddell were abnormally high because of enzymatic hydrolysis of morphine conjugates by microbes after death is just speculation.

What is more troublesome about Dr. Karch's postcard from America is that he neglects to mention anywhere in the article that he was hired as an expert witness for the defence in the Dr. Moor trial. Failure to divulge this information renders his opinions suspect.

Dr. Karch proceeds to question whether post-mortem drug concentration should ever be converted into the dose of drug administered. This is not exactly big news for forensic toxicologists for a host of reasons, many of which were discussed in a recent review article.[8] To exemplify this problem, Karch considers the recreational drug methamphetamine. He cites a controlled dosing study with 10 healthy volunteers each of whom received a 10 mg oral dose of methamphetamine. The plasma concentration-time profiles were used to derive the apparent volumes of distribution (V_d) of methamphetamine and according to Karch these ranged from 2 to 11 L/kg between subjects.[9]

A closer examination of the article concerned shows that only seven volunteer subjects were involved and the distribution volumes of methamphetamine averaged 5.8 L/kg and ranged from

1752-928X/$ - see front matter
doi:10.1016/j.jflm.2009.04.012

1.6 to 8.9 L/kg (Table 1 in the article, p. 125). Karch then proceeds to calculate that for a 70 kg male with a concentration of methamphetamine in blood of 20 ng/mL the dose taken might range from 0.2 mg (V_d = 2 L/kg) to 1.6 mg (V_d = 11 L/kg).

According to my own calculations these values should be 2.8 mg (V_d = 2 L/kg) or 15.4 mg (V_d = 11 L/kg) and, needless to say, these represent the amounts of methamphetamine absorbed and distributed in all body fluids and tissues and not the dose of drug administered. Calculations of this nature cannot possibly give reliable results without knowledge of the bioavailability of the drug after oral intake. Furthermore, in connection with recreational drug use and abuse nothing is usually know about the purity of the substance taken, which is another confounding factor.

In criminal trials in which complex medical or forensic evidence is presented and explained to the jury great care is necessary not to confuse the issue. This becomes problematic when expert witnesses hired by either side in the case voice completely different opinions. How can juries decide when experts disagree? More widespread use of court appointed experts would help to eliminate the oft partisan atmosphere in a criminal trial (adversarial system) and battles between the experts. As suggested elsewhere, many expert witnesses are hired guns willing to testify to anything for a fee or crackpots often with an advanced degree from a respectable university.[10]

Conflict of Interest

None declared.

Funding

No funding.

Ethical approval

No ethical approval is needed.

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Available online 10 May 2009